REMARKS

Claims 19-22, 25-59 and 62-65 are pending.

1. Double Patenting Rejection:

Claims 19-22, 25-59 and 62-68 remain provisionally rejected under obviousness-type double patenting over claims 1-11 of co-pending U.S. Application No. 10/277,764. It is the opinion of the Examiner that although the claims are not identical, they are not patentably distinct from each other because they are both drawn to treatment of disease using immunoglobulin fusion proteins. For the reasons set forth below, Applicant respectfully disagrees with Examiner's interpretation and requests withdrawal of the double patenting rejection.

It is certain that both inventions involve immunotherapy techniques for treatment of related immune disorders. However, that is the extent of the similarity, which is overshadowed by the diversity between the mechanistic features of the two distinct inventions.

The '277 application claims use of an immunomodulating agent which is comprised of an Fc receptor ligand and a T-cell receptor agonist, where the treatment results in reduction of inflammatory reactions or suppression of inflammatory cytokine production. On the other hand, Applicant's present invention claims use of a fusion protein, comprising an immunoglobulin linked to an antigen responsible for the disease to be treated. These are two separate and distinct compositions, with each composition achieving an independent approach to treating immune disorders. Moreover, the mechanism of action of Applicant's invention involves crosslinking Fc receptors present on the cell surface of APCs, while the '277 application focuses on a more indirect method of treatment by suppressing or reducing the T-cell mediated response. Thus, not only are the conflicting claims patentably distinct from each other, they are mechanistically distinct based on their therapeutic approach. Furthermore, Applicant's present invention involves a fusion protein comprised of an immunoglobulin linked to a disease specific antigen, which is completely distinct from the joint therapy approach of using at least one Fc receptor ligand and at least one T-cell receptor agonist in order to affect inflammatory responses, as claimed by the '277 application.

These allegedly conflicting claims are not, as argued by Examiner, both drawn to treating diseases with immunoglobulin fusion proteins. Applicant's present invention is the only one claiming use of a fusion protein in such a manner. The '277 application relies on an entirely different mechanistic approach to treating immune disorders. The '277 invention claims use of one or more of two separate pieces (ligand + agonist) in order to reduce T-cell mediated inflammatory reaction and suppress inflammatory cytokine production. Not only is this not a fusion protein, but its method of treatment differs from that of Applicant's present invention as claimed. As such, Applicant respectfully requests Examiner to withdraw the double patenting rejection based on the above proffered arguments which differentiate the involved claims.

2. Rejection of Claims Based on §112, 1st paragraph

The pending claims in the present application stand rejected under §112, 1st paragraph. The Examiner, at paragraph 5 from the Office Action mailed June 16, 2005, finds that the claims contain subject matter not described in the specification to reasonably convey to one skilled in the relevant art that the inventor had possession of the claimed invention. Based on the argument submitted below and the claims as presently amended, Applicant respectfully requests Examiner to withdraw the rejection under §112, 1st paragraph.

It is not necessary for the subject matter of the claims to be described literally in the specification. In re Lukach, 169 U.S.P.Q. 795, 796 (C.C.P.A. 1971) Rather, it is sufficient that the specification convey clearly to those skilled in the art that the Applicant invented the specific subject matter later claimed. In re Wertheim, 191 U.S.P.Q. 90, 97 (C.C.P.A. 1976) The written description requirement is separate and distinct from the enablement requirement. See, e.g., Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1560, 19 U.S.P.Q. 2d 1111, 1114 (Fed. Cir. 1991); see also University of Rochester v. G.D. Searle & Co., 358 F.3d 916, 920-23, 69 U.S.P.Q. 2d 1886, 1890-93 (Fed. Cir. 2004) (discussing history and purpose of the written description requirement); In re Curtis, 354 F.3d 1347, 1357, 69 U.S.P.Q. 2d 1274, 1282 (Fed. Cir. 2004) ("conclusive evidence of a claim's enablement is not equally conclusive of that claim's satisfactory written description") An invention may be described without the disclosure being enabling (e.g., a chemical

compound for which there is no disclosed or apparent method of making), and a disclosure could be enabling without describing the invention (e.g., a specification describing a method of making and using a paint composition made of functionally defined ingredients within broad ranges would be enabling for formulations falling within the description but would not describe any specific formulation). See In re Armbruster, 512 F.2d 676, 677, 185 U.S.P.Q. 152, 153 (C.C.P.A. 1975) ("[A] specification which 'describes' does not necessarily also 'enable' one skilled in the art to make or use the claimed invention.")

An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 U.S.P.Q. 2d 1961, 1966 (Fed. Cir. 1997) Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention. See, e.g., Pfaff v. Wells Electronics., Inc., 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 U.S.P.Q. 2d 1641, 1647 (1998); University of California v. Eli Lilly, 119 F.3d 1559, 1566, 43 U.S.P.Q. 2d 1398, 1404 (Fed. Cir. 1997), cert. denied, 523 U.S. 1089 (1998).; Amgen, Inc. v. Chugai Pharmaceutical, 927 F.2d 1200, 1206, 18 U.S.P.Q. 2d 1016, 1021 (Fed. Cir. 1991) (one must define a compound by "whatever characteristics sufficiently distinguish it"). "Compliance with the written description requirement is essentially a fact-based inquiry that will 'necessarily vary depending on the nature of the invention claimed.'" Enzo Biochem, Inc. v. Gen-Probe, Inc., 323 F.3d 956, 969-70, 63 U.S.P.Q. 2d 1609, 1617 (Fed. Cir. 2002)

For some biomolecules, examples of identifying characteristics include a sequence, structure, binding affinity, binding specificity, molecular weight, and length. Although structural formulas provide a convenient method of demonstrating possession of specific molecules, other identifying characteristics or combinations of characteristics may demonstrate the requisite possession. For example, disclosure of an antigen fully

characterized by its structure, formula, chemical name, physical properties, or deposit in a public depository provides an adequate written description of an antibody claimed by its binding affinity to that antigen. Noelle v. Lederman, 355 F.3d 1343, 1349, 69 U.S.P.Q. 2d 1508, 1514 (Fed. Cir. 2004) (holding there is a lack of written descriptive support for an antibody defined by its binding affinity to an antigen that itself was not adequately described)

Claims 19-22, 25-59 and 62-65 are directed to methods of alleviating symptoms associated with specified autoimmune diseases. These autoimmune diseases are selected from the group comprising multiple sclerosis, insulin dependent diabetes and rheumatoid arthritis. Further, the claims also detail the composition to be used to alleviate said symptoms, to wit, said immunoglobulin linked to said antigen. The specification discloses how the fusion construct is to be assembled. Finally, Applicant also delineates the claimed fusion protein from what is known in the art.

Applicant has ample support in the specification for the invention as set forth in the claims. For instance, in the specification at [0024], Applicant identifies myelin antigens, such as those presented on myelin basic protein (MBP) and proteolipid protein (PLP), to which T-cells are targeted. These are but one example of antigens known by skilled artisans in the field. Another example is found at [0047] in the specification, where the disclosure of Falcone et al., as incorporated by reference, shows antigens such as keyhole limpet hemocyanin (KLH) and MBP as being mechanistically associated with an autoimmune disease. Furthermore, heat shock proteins (e.g. HSP65, dnaJP1) have been found important agents of antigen-specific immune therapy for rheumatoid arthritis. These examples of immunogens are sufficient to adequately describe the claimed invention, as it is not necessary to disclose the structure and identity of all antigens associated with the autoimmune diseases found in the claims. It is only necessary that Applicant convey clearly to those skilled in the art that Applicant invented the specific subject matter later claimed. As such, by disclosing several antigens which are responsible for the specified autoimmune diseases, in addition to describing the immunoglobulin, it will have been necessarily conveyed, in a clear manner to those skilled in the art, that Applicant invented the specific subject matter later claimed. Applicant did more than merely show possession of a fusion protein capable of reducing

disease symptoms in individuals suffering from an autoimmune disease. Applicant disclosed how the individual components of the fusion protein were to be utilized, how the fusion protein was assembled and, through experimental data, displayed the impact the fusion protein had on the selected target.

Examiner also takes issue with the fact that the claims do not require the antigen be specific for autoreactive T cells associated with the autoimmune disorders, just that it is "involved in said autoimmune diseases". Applicant hereby acknowledges Examiner's argument and has resolved such issue by way of amendment.

Thus, based on the above proffered arguments and by amending the claims to describing said antigens as those specific for autoreactive T cells associated with said autoimmune disease, rather than merely involved in said autoimmune disease, Applicant has clarified the claimed invention sufficient to overcome the Examiner's argument. Applicant has respectfully obliged Examiner's request to give some description of the antigen in the claims and respectfully requests the withdrawal of the rejection under §112, 1st paragraph for claims 19-22, 25-59 and 62-65.

Applicant also acknowledges Examiner's note that the claims recite insulin dependent diabetes but some Type II diabetic patients are insulin dependent. Applicant hereby acknowledges Examiner's argument and has resolved such issue by amending the relevant claims to read "Type 1 diabetes mellitus" rather than "insulin dependent diabetes".

Examiner has also rejected claims 34, 49 and 64, specifically, for failing to meet the requirements of §112, 1st paragraph. The Examiner argues that in order to be commensurate with the scope of the claims, all of the antigens for every disease, as well as all the diseases, to be treated by decreasing IFN-gamma and increasing IL-10 must be known. Moreover, Examiner further opines that Applicant has failed to meet this standard because Applicant had described only a particular number of diseases to be treated and a certain number of antigens to be used to treat said diseases.

In the allegedly "predictable" fields of technology, such as the mechanical arts, a single embodiment of the invention may provide broad enablement that is sufficient to support broad claims. MPEP §2164.08. By contrast, in the so-called "unpredictable" arts, such as the biotechnological arts, the scope of enablement varies inversely with the

degree of unpredictability of the technology involved. In re Fisher, 166 U.S.P.Q. 18, 24 (C.C.P.A. 1970); Enzo Biochem, Inc. v. Calgene, Inc., 52 U.S.P.Q.2d 1129, 1138 (Fed. Cir. 1999) Without delving into the degree of unpredictability of Applicant's invention, even in such "unpredictable" arts, applicants are not required to disclose every species encompassed by their claims. In re Angstadt, 190 U.S.P.Q. 214, 218 (C.C.P.A. 1976) Nonetheless, sufficient disclosure must exist, either through illustrative examples or terminology, to teach those of ordinary skill how to make and use the invention as broadly as it is claimed. In re Vaeck, 20 U.S.P.Q.2d 1438, 1445 (Fed. Cir. 1991)

In the present case, Applicant has identified a fusion protein, described the details of said fusion protein and showed how precisely the construct will alleviate disease symptoms in patients. Moreover, the mechanism of action by which the fusion protein will operate is sufficiently disclosed, both by examples and terminology, to teach those skilled in the art how to use Applicant's invention. By modulating the levels of IFN-gamma and/or IL-10, Applicant's fusion protein will reduce disease symptoms for patients in need of such treatment. It is not necessary to know all the antigens for every disease to be treated in the same manner as described by Applicant. Nor is it essential to know all of the diseases to be treated in like manner. Examiner has reasoned only by accomplishing such intimate knowledge of all antigens and diseases will Applicant be allowed the invention as claimed. However, the claims now define the antigen as being specific for autoreactive T cells associated with the respective autoimmune disease. Thus, it is not merely that the antigen is "associated" with the autoimmune disease, but the requisite specificity has now been increased by way of amendment to have the antigen being specific for autoreactive T cells associated with the autoimmune disease in question. Therefore, Applicant respectfully requests Examiner withdraw the previous rejection with respect to claims 34, 49 and 64 under §112, 1st paragraph, as any defect was cured by way of amendment and in light of the above offered arguments.

3. Rejection of Claims Based on § 102(b) Reference

Examiner has rejected claims 34-57, 43-52 and 58-68 under § 102(b) as being anticipated by WO 90/09804. Examiner has noted the '804 patent ("Zanetti") teaches autoimmunity achieved through administration of Ig fusion proteins with antigens so as

to induce tolerance. Further, Examiner argues that the Ig constructs as taught by Zanetti appear to have the same structure as Applicant's invention as claimed. For the arguments put forth below, Applicant respectfully finds the invention as claimed is not anticipated by Zanetti and respectfully requests Examiner to withdraw the rejection under §102(b).

Zanetti teaches used of engineered immunoglobulins to induce an immune response in conjunction with an epitope and to build tolerance to antigens (Zanetti application, p.1). The goal of Zanetti's invention is to create a vaccine which may be against autoimmune disorders. For example, Zanetti focuses the present invention to "pharmaceutical compositions containing, as essential pharmaceutical principal, a novel immunoglobulin hereof, particularly those in the form of an administratable pharmaceutical vaccine." (Zanetti, p.5) Likewise, the proffered examples put forth in the specification of the Zanetti application deal with generating antibodies to the delivered antigen, which is necessary in the creation of a vaccine, allowing such a strategy to be "exploited to render a B-cell epitope T-independent, proving its utility...for the development of new antibody vaccines, for example, as an alternative to peptide based vaccines." (Zanetti, p.23-24)

It seems clear that Zanetti chose to confront autoimmune disorders through a different mechanism than that claimed by Applicant. In fact, Zanetti only theorizes about using engineered immunoglobulins as methods of treatments for autoimmune disorders. Zanetti discloses use of such immunoglobulins "for building tolerance to certain antigens, including those associated with autoimmune diseases, or for down regulating hypersensitivity to allergens." (Zanetti, p.5) The only other mention of the mechanism of Zanetti is in the abstract, where Zanetti speculates such "epitope containing immunoglobulins are useful in treating such diseases as autoimmune disorders, as the epitope inserted into the binding domain of the immunoglobulin is capable of inducing or preventing sensitization of the host to that epitope." (Zanetti, Abstract)

Zanetti indeed describes use of immunoglobulins to either build tolerance to certain antigens or for downregulating hypersensitivity to allergens. Zanetti mentions nothing regarding use of immunoglobulins as part of a fusion construct with an antigen responsible for an autoimmune disorder to aid in treating an individual suffering from said autoimmune disorder. Zanetti is dedicated to a vaccine approach as its mechanism

of action to treat an autoimmune disorder. Zanetti relies on building tolerance against whatever epitope is delivered, whereas Applicant's invention relies on a fusion protein capable of crosslinking Fc receptors on the cell surfaces of antigen presenting cells as its mechanism of action. Moreover, there is no mention in Zanetti of use of a T-cell agonist for presentation on the surface of an antigen presenting cell, which results in the induction of inactivation of autoreactive T-cells, downregulation of the immune system and amelioration of any associated autoimmune disease.

Finally, Zanetti does not, in fact, disclose a construct in which an immunoglobulin is linked to an antigen. Specifically, a heavy chain of the engineered antibody of Zanetti has the structure:

V1—(foreign epitope)—V2—C

where V1 is the portion of the variable region preceding the introduced foreign epitope at CDR3; V2 is the portion of the variable region following the introduced foreign epitope and; C is the constant region. This is not the same as Applicant's invention, which consists of having an immunoglobulin or a portion thereof linked to an antigen. Furthermore, Zanetti claims a construct where the epitope is surrounded by non-modified immunoglobulin sequences on both sides in a single polypeptide chain. This is quite dissimilar to Applicant's invention, which does involves an alteration of the insertion region itself. Specifically, Applicant's invention involves the *deletion* of the heavy chain CDR3 loop and replacing it with nucleotide sequences coding for the selected peptide. Zanetti, on the other hand, introduced a foreign eptiope *into* the CDR3 of the heavy chain of a chimeric antibody. This is yet another distinction between Zanetti and the claimed invention.

In order to be a proper § 102 (b) rejection, every element of the claim must be present in the cited reference. Richardson v. Suzuki Motor Co., 868 F.2d 1226, 1236, 9 U.S.P.Q.2d, 1913, 1920 (C.A.F.C. 1989); MPEP 2131 Therefore, every element of claims 34-57, 43-52 and 58-68 must be present in Zanetti to be a valid § 102(b) reference. This is certainly not the case, as use of immunoglobulins in a vaccine capacity is quite different than Applicant's proposed mechanism by which the fusion construct of the claimed invention is capable of modulating IFN-gamma and IL-10 levels, thereby

reducing disease symptoms in a unique manner relative to Zanetti. Moreover, Zanetti does not disclose a construct in which an immunoglobulin is linked to an antigen. This is too broad a description of Zanetti's construct, as Applicant has engineered the claimed invention much differently, as described supra.

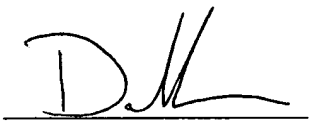
Accordingly, Applicant respectfully requests Examiner to withdraw the rejection under § 102(b) based on the above arguments and concurrent amendments to the claims.

4. Rejection of Claim 25 Based on § 1.75(c)

Examiner has objected to the form of claim 25 under § 1.75(c) as being of improper dependent form. Applicant has cancelled claim 25 and requests Examiner to withdraw the § 1.75(c) rejection as the issue is now moot.

Applicant respectfully requests withdrawal of the above identified rejections and allowance of the present application based on Applicant's arguments and amendments. Applicant is applying for a one month extension of time and a Request for Continued Examination. If there are any questions or comments, Applicant's attorney may be reached at the telephone number state below.

Respectfully submitted,



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